DETAILED ACTION

Applicant's Arguments

Applicant's arguments, filed August 17, 2011, have been fully considered but they are not deemed persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims under Examination

Claims 1-15, 19, and 20 have been canceled. Claims 17, 18, and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Accordingly, the claim herein under examination is claim 16. It is noted that the instant claim is examined in accordance with the elected species of Ca++ porter and the gene SRCAP as elected in the '*Response*', filed in the October 29, 2010.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

U.S. Patent Number 7,452,670 in view of Duchen

The rejection of claim 16 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,452,670 (herein "U.S. Patent '670") in view of Duchen, M.R. (Roles of Mitochondria in Health and Disease. Diabetes. Vol. 53, Supplement 1, February 2004, pages S96-S102 (herein 'Duchen') is maintained for reasons of record.

In the '*Response*' (page 5, line 27 to page 6, line 14), filed August 17, 2011, Applicant argues: 1) US PAT '670 does not suggest using ruthenium red as a means to suppress alpha synuclein-meditated toxicity"; and 2) Duchen fails to resolve the deficiency in US PAT '670, wherein Duchen provides for "only a general statement that mitochondrial dysfunction has been implicated in Parkinson's disease". Specifically, that "nothing in Duchen would have led the person of ordinary skill in the art to reasonably expect that mitochondrial calcium would be relevant to Parkinson's disease and that ruthenium red would be effective at suppressing alpha synuclein-mediated toxicity". However, Applicant's arguments are unpersuasive for the reasons discussed below.

Claim 16 is considered unpatentable over claim 1 of US PAT '670 in view of Duchen. For instance, claim 1 of US PAT '670 is drawn to "[a] method of identifying an agent for diminishing cellular toxicity associated with an α-synuclein polypeptide of Parkinson's disease, comprising: contacting a yeast cell with a candidate agent, wherein the yeast cell expresses an α synuclein polypeptide and the cell does not express an endogenous wild-type gene, wherein the absence of the endogenous wild-type gene expression causes or enhances toxicity associated with the presence of the α synuclein polypeptide, and wherein the endogenous wild-type gene is selected from glo4 and gtt1; and determining whether the candidate agent reduces toxicity of the α synuclein polypeptide." Similarly, claim 16 of the instant application is drawn to "[a] method of identifying a compound that inhibits synuclein (aS) mediated toxicity, the method comprising: providing a yeast cell expressing an amount of aS that reduces viability of the cell; contacting the cell with a candidate agent selected from the group consisting of

a fungicide, lipoxygenase inhibitor, prostaglandin synthetase inhibitor, membrane detergent, electron transporter, mitochondrial Ca++ porter, toxic anion, and antibiotic; and determining whether the candidate agent enhances viability of the cell, to thereby identify a compound that inhibits aS mediated toxicity."

As recited above, US PAT '670 claims a method of identifying an agent for diminishing cellular toxicity associated with α-synuclein polypeptide of Parkinson's disease. By way of definition, US PAT '670 provides various applicable wild-type genes, such as SRCAP (Col. 14, line 43 to Col. 15, line 26). However, US PAT '670 fails to teach "contacting the cell with a candidate agent...mitochondrial Ca++ porter" (instant claim 16).

Duchen investigates the role mitochondria play in the mammals and indicates that damage to mitochondria inevitably leads to disease, wherein mitochondrial defects have been implicated as a mechanism of aging and age-related disease (page S97, left column, lines 8-32). The authors state "mitochondrial dysfunction has been implicated in all the major neurodegenerative diseases - Parkinson's, Alzheimer's, motor neuron disease" (*Id.*). Duchen discusses and elaborates on the cellular calcium signaling in regulating/controlling mitochondrial function, wherein calcium is carried into the mitochondrion through an electrogenic uniporter down an electrochemical potential gradient whenever the concentration of extramitochondrial calcium rises (page S97, right column, lines 9-24). The electrogenic uniporter is indicated as being blocked by ruthenium red (i.e. mitochondria Ca++ porter) (*Id.*).

Although the conflicting claims are not identical, wherein US PAT '670 does not specifically recite the combination of the disclosed method with a candidate agent such

as mitochondrial Ca++ porter (claim16), they are not patentably distinct from each other. Duchen indicates: 1) mitochondria dysfunction is associated with neurodegenerative diseases (i.e. Parkinson's); 2) calcium uptake in mitochondria is regulated by an electrogenic uniporter; and 3) said electrogenic uniporter is known to be regulated (i.e. blocked) by ruthenium red. Since US PAT '670 and Duchen teach the same outcome and/or purpose, the study of neurodegenerative diseases, one of ordinary skill in the art would have had a reasonable expectation of success to determine whether ruthenium red is a candidate agent that enhances viability of a cell (i.e. inhibit alpha synuclein) by combining the teachings of US PAT '670 with that of Duchen..

Thus, US PAT '670 in view of Duchen renders the instant claim unpatentable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject

matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

It is noted that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf). The combination of prior art cited above in all rejections under 35 U.S.C. 103 satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this

has been accomplished the holdings in KSR can be applied (*KSR International Co. v. Teleflex Inc. (KSR)*, 550 USPQ2d 1385 (2007): "Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention."

U.S. Patent No. 7,452,670 in view of Duchen et al.

The rejection of claim 16 under 35 U.S.C. 103(a) as being obvious over U.S. Patent Number 7,452,670 (herein ‘‘US PAT ’670”) in view of Duchen, M.R., Roles of Mitochondria in Health and Disease. Diabetes. Vol. 53, Supplement 1, February 2004, pages S96-S102 (herein ‘Duchen’) is herein maintained for reasons of record.

In the ‘*Response*’ (page 6, lines 21-26), filed August 17, 2011, Applicant argues that “US PAT ‘670 and Duchen do not render claim 16 obvious for the same reasons provided in response to the double patenting rejection”. As taken from the above

double patenting rejection, Applicant argues: 1) US PAT '670 does not suggest using ruthenium red as a means to suppress alpha synuclein-meditated toxicity"; and 2) Duchen fails to resolve the deficiency in US PAT '670, wherein Duchen provides for "only a general statement that mitochondrial dysfunction has been implicated in Parkinson's disease". In particular, Applicant asserts that "nothing in Duchen would have led the person of ordinary skill in the art to reasonably expect that mitochondrial calcium would be relevant to Parkinson's disease and that ruthenium red would be effective at suppressing alpha synuclein-mediated toxicity". However, Applicant's arguments are unpersuasive for the reasons discussed below.

US PAT '670 is herein applied from the above double patenting rejection, wherein US PAT '670 discloses and claims (i.e. claim 1) a method of identifying an agent for diminishing cellular toxicity associated with α-synuclein polypeptide of Parkinson's disease (Abstract; instant claim 16). Generally, the method includes the steps of: 1) contacting yeast cell expressing α-synuclein with a candidate agent; and 2) determining whether the candidate agent reduces α-synuclein toxicity (*Id.*; Col. 2, lines 25-38; and Col. 3, lines 45-61). Further, the inventors list various applicable wild-type genes, which includes SRCAP (Col. 14, line 43 to Col. 15, line 26). Example 1 describes the identification of targets and molecular mechanisms of α-synuclein in yeast through a collection of mutants that have been previously used to identify gene pathways in human mitochondrial diseases. While US PAT '670 does disclose the use of candidate agents for testing to be synthetic or natural compounds (Col. 3, lines 29-34), it is acknowledged that US PAT '670 does not specifically teach contacting the cell with a mitochondrial Ca++ porter (instant claim 16).

Duchen resolves the failed specific teaching of contacting a cell with mitochondrial Ca++ porter in the method disclosed in US PAT '670. Duchen investigates the role mitochondria plays in mammals and indicates that damage to mitochondria inevitably leads to disease, wherein mitochondrial defects have been implicated as a mechanism of aging and age-related disease (page S97, left column, lines 8-32). The authors state "mitochondrial dysfunction has been implicated in all the major neurodegenerative diseases - Parkinson's, Alzheimer's, motor neuron disease" (*Id.*). Duchen discusses and elaborates on the cellular calcium signaling in regulating/controlling mitochondrial function, wherein calcium is carried into the mitochondrion through an electrogenic uniporter down an electrochemical potential gradient whenever the concentration of extramitochondrial calcium rises (page S97, right column, lines 9-24). The electrogenic uniporter is indicated as being blocked by ruthenium red (i.e. mitochondria Ca++ porter) (*Id.*).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize ruthenium red (i.e. mitochondria Ca++ porter) as described in Duchen as a candidate agent in the method of screening candidate agents to identify lead compounds for the development of therapeutic agents for the treatment of neurodegenerative diseases (i.e. Parkinson's) of US PAT '670 because US PAT '670 and Duchen have the same outcome and/or purpose, wherein both of the cited references are directed to the study of neurodegenerative diseases. Furthermore, one of ordinary skill in the art would have been led and would have had a reasonable expectation of success to utilize ruthenium red as a candidate agent that enhances viability of a cell (i.e. inhibit alpha synuclein) based upon the teaching in Duchen of: 1)

mitochondria dysfunction is associated with neurodegenerative diseases (i.e. Parkinson's); 2) calcium uptake in mitochondria is regulated by an electrogenic uniporter; and 3) said electrogenic uniporter is known to be regulated (i.e. blocked) by ruthenium red.

Thus, US PAT '670 in view of Duchen renders the instantly claimed invention unpatentable.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is 571-270-7464. The Examiner can normally be reached on Monday - Thursday; 7:30am-5pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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